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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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FOLEY HOAG, LLP/WYETH
PATENT GROUP, (w/WYS)
155 SEAPORT BLVD.
BOSTON, MA 02210-2600

EXAMINER	
GAMBEL, PHILLIP	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/501,102	CO ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *145,147 and 149-154* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *145, 147 and 149-154* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/07/2008, 12/04/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/04/2008 has been entered.

Applicant's amendment, filed on 12/04/2008, has been entered.

Claims 145 and 154 have been amended.

Claims 1-144, 146, 148 and 155-160 have been canceled previously.

Claims 145, 147 and 149-154 are pending.

Again for the record and as indicated previously, claims 145, 147 and 149-154, as they read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

Also, as noted previously, the previously amended recitation of administering an additional (third) agent, is read on administering cyclosporin or rapamycin as the additional (third) agent only.

Accordingly, the third agents other than cyclosporin or rapamycin are withdrawn from consideration as being directed to a non-elected invention. See 37 C.F.R. 2(b) and M.P.E.P. 821.03.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Action will be in response to applicant's arguments, filed 12/04/2008.

The rejections of record can be found in the previous Office Actions, mailed 04/10/2006, 11/06/2006 and 05/07/2007, 06/25/2007, 10/09/2007 and 04/08/2008

3. Priority.

Applicant's arguments, filed 12/04/2008, and the examiner's position on the priority of the instant claims are essentially the same of record.

Currently, applicant's arguments rely upon the following.

Applicants respectfully traverse the objection. In Applicants' response to the Non-Final Office Action, dated October 9, 2007, claims 145 and 154 were amended deleting the phrase, "inhibitor or the CD40/CD40 ligand costimulatory interaction." Applicants believe the Examiner's objection is considered moot and therefore respectfully request reconsideration and withdrawal of the objection.

Here, again, applicant's arguments have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant's arguments have not been found persuasive for the reasons of record and again, reiterated herein for applicant's convenience.

The effective filing date of the instant claims is deemed as follows.

As addressed previously and reiterated / addressed herein for applicant's convenience, it appears that applicant is relying upon limited species, namely
"α CD40 ligands" in USSN 08/249,011 though it is not clear what "α CD40 ligands" was intended to mean, since this does not appear to be a designation of art or
"anti-CD40 antibodies" in USSN 09/339,596
as the only designations of possible inhibitors of CD40:CD40 ligand interactions clearly described in the priority documents.

Currently, the claims recite both "anti-CD40 antibody" and "anti-CD40 ligand antibody" as not being administered to the transplant recipient.

Also, as pointed out previously, applicant's amended claims, filed 09/25/2007, which included the recitation of the Markush of
"(third) agents selected from the group consisting of: calcineurin inhibitor, steroid, and immunosuppressive agent that arrest the growth of immune cells, methotrexate, transplant salvage pathway inhibitor, IL-2 receptor antagonist, and analogs thereof, and wherein an inhibitor of the CD40/ CD40 ligand costimulatory interaction is not administered to the transplant recipient"
are not readily apparent in applicant's priority documents USSNs 09/339,596 and 09/249,011, particularly the written description of
"calcineurin inhibitor", "immunosuppressive agent that arrest the growth of immune cells", "transplant salvage pathway inhibitor", "IL-2 receptor antagonist" and "analogs" in addition to "anti-CD40 antibody" and "anti-CD40 ligand antibody".

If applicant desires priority back to their priority documents,
applicant is invited to point out and provide documentary support for the priority of the instant claims

Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

A claim as a whole has only one effective filing date.
See Studiengelsellschaft Kahle m.b.H. v. Shell Oil Co. 42 USPQ2d 1674, 1677 (Fed. Cir 1997).

Applicant's arguments and amended claims have not been found persuasive for providing sufficient written description for the claimed "(third) agents", including the negative limitation encompassing both "anti-CD40 antibody" and "anti-CD40 ligand antibody" as well as "calcineurin inhibitor", "immunosuppressive agent that arrest the growth of immune cells", "transplant salvage pathway inhibitor", "IL-2 receptor antagonist" and "analogs" in applicant's priority documents USSNs 09/339,596 and 09/249,011.

The priority of the instant claims is deemed to be the filing date of the instant application USSN 09/501,102.

4. Claim 154 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 154 is indefinite in the recitation of "modulating" because the claims fails to state the function which is to be achieved. The term "modulating" is relative in nature, which renders the claims indefinite. The term "modulating" is not defined by the claims; the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention

It is suggested to amend the claim to recite the particular characteristics of "modulating" intended, including the parameters and direction of such "modulation", by setting forth testable functions, provided there is written description in the specification as filed.
Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

5. Upon reconsideration of applicant's amended claims, filed 12/04/2008, the previous rejection under 35 U.S.C. § 112, first paragraph, written description has been withdrawn.

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language

(f) he did not himself invent the subject matter sought to be patented.

7. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Response to Applicant's Arguments based upon the Gray Declaration filed under 37 CFR 1.132 on Prior Art Rejections.

Applicant's arguments in conjunction with the Gray Declaration filed under 37 CFR 1.132, filed 12/04/2008, have been fully considered but have not been found convincing for the reasons herein as they address the Gray Declaration and for the reasons of record reiterated below for applicant's convenience.

The Gray Declaration filed under 37 CFR 1.132 includes the following.

I, Gary S. Gray, a citizen of the United States, residing at 32 Milton Road, Brookline, Massachusetts 02445, hereby declare as follows:

1. I am a co-inventor in the above-referenced patent application, along with co-inventors Man Sung Co, Maxmiliano Vasquez, Beatriz Carreno, Abbie Celniker, Mary Collins, Samuel Goldman, Andrea Knight, Denise O'Hara, Bonita Rup, Geertruida Veldman, Garvin Warner and Stuart Friedrich.

2. I understand that U.S. Patent No. 6,605,279 by Freeman et al. was cited against the above-referenced patent application.

3. I am a co-inventor with Gordon J. Freeman and Lee M. Nadler of U.S. Application No. 09/425,762, filed October 22, 1999, which issued as U.S. Patent No. 6,605,279.

4. I conceived of the invention as described and claimed in the above-identified application, prior to the earliest priority date, e.g., July 26, 1993, of U.S. Patent No. 6,605,279.

In contrast to applicant's submission of the Gray Declaration under 37 CFR 1.132, it appears to be an attempt to obviate the prior art via conception (and possibly diligence and reduction to practice) that is appropriate under 37 CFR 1.131 and not under 37 CFR 1.132.

In turn, given the indication that Gray 1.132 declaration may be considered as a 1.131 declaration.

The 1.131 declaration (Gray 1.132 declaration) is deficient for several reasons.

To antedate a reference, one must provide either a reduction to practice before the effective date or show conception coupled with diligence to subsequent reduction of practice or to the filing date of the application.

At most, the Gray Declaration declares conception and does not address diligence nor subsequent reduction to practice.

No objective evidence has been provided to support even the conception asserted in the Gray Declaration.

Furthermore, the rule requires an averment that the invention was made in the United States (versus France). The rule requires that copies of drawings or other records must accompany and form part of the affidavit or declaration or their absence satisfactorily explained.

For example, a mere statement that the invention was reduced to practice or that the applicant exercised conception, due diligence or reduction to practice is not enough to satisfy the rule.

Absent a clear explanation of providing exactly what facts are relied upon by applicant, the Gray Declaration provides little assistance in enabling the PTO to determine applicant's assertions of conception, diligence and reduction to practice before the prior art.

All of the current inventors have not signed the declaration (or an appropriate 1.131 declaration).

In addition, the Gray Declaration indicates that Gray is the sole person responsible for conception, which raises the ambiguity who is the inventor of the instant application.

Alternatively, if the Gray 132 Declaration is an attempt to indicate that Gray conceived of the subject matter disclosed but not claimed in U.S. patent No. 6,605,279, the following is noted.

In response to the prior art rejections, applicant argues the following.

Applicants respectfully traverse the rejection. Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 by co-inventor Dr. Gary S. Gray. The Declaration states that Dr. Gray conceived of the subject matter disclosed (and not claimed) in U.S. Patent No. 6,605,279, which is relied upon in the pending rejection, thereby removing the '279 patent as a valid § 102(e) reference. Applicants believe this renders the Examiner's rejection moot. Applicants therefore respectfully request reconsideration and withdrawal of the rejection.

Applicant's arguments that the Gray Declaration states Gray conceived of the subject matter disclose but not claimed in U.S. Patent No. 6,605,279 is not consistent with the Gray Declaration itself.

For example, there is not a clear statement by Gray that he conceived of all of the subject matter disclosed but not claimed in U.S. Patent No. 6,605,279.

More importantly, the Gray Declaration does not clearly indicate what parts of the disclosure of U.S. Patent No. 6,605,279 are solely Gray's conception.

Also, it is noted that the claims of U.S. patent No. 6,605,279 are drawn to the combination of anti-B7-1 antibodies and anti-B7-2 antibodies in a compositions for administration and in pharmaceutically acceptable carriers.

In turn, it is the combination of anti-B7-1 antibodies and anti-B7-2 antibodies that is critical to the instant claimed methods of treating transplant rejection in the instant application.

Note that the elected species of cyclosporin as the third agent in the instant methods has been conventional in transplantation regimens since at least the early 1980's.

Further, a fair reading of the claimed invention of U.S. patent No. 6,605,279 would indicate that the combination of anti-B7-1 antibodies and anti-B7-2 antibodies are administer for the disclosed utilities, including those of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34 of U.S. patent No. 6,605,279).

If as applicant asserts, the Gray Declaration asserts conception as it reads on U.S. patent No. 6,605,279,

then it would appear that Gray Declaration is asserting the inventorship of a U.S. Patent is not correct.

U.S. patents are presumed valid by U.S. courts unless proven otherwise. See 35 U.S.C. 282.

Further, the assertion that the Gray Declaration asserts conception / inventorship on all of the disclosed description in the Freeman et al. U.S. Patents are inconsistent with a number of Freeman et al. U.S. Patents in the prior art family that include Gray as an inventor.

For example, see U.S. Patent Nos. 5,942,607; 6,084,067 (1449; #AG); 6,130,316; 6,824,779, 7,459,544 in addition to U.S. patent No. 6,605,279,

Rather, a fair reading of the statement as follows, "4. I conceived of the invention as described and claimed in the above-identified application, prior to the earliest priority date, e.g., July 26, 1993, of U.S. Patent No. 6,605,279" could be a reading on conceiving the invention as described and claimed in the above-identified application as the current USSN 09/501,102 and not as U.S. Patent No. 6,605,279.

It is noted that the prior art rejections are based upon a reference to the U.S. Patent and not the application per se.

In turn, it is the instant application that is the document being referred to as an application.

Given the ambiguities and a lack of clear information and statement of facts associated with the Gray Declaration,

Applicant's arguments in conjunction with the Gray Declaration have not been found convincing to overcome the prior art rejections of record.

9. Claims 145, 147 and 149-154 are rejected under 35 U.S.C. § 102(f) because the applicants did not invent the claimed subject matter.

The Gray Declaration under 37 CFR 1.132, filed 12/04/2008, declares the following.

4. I conceived of the invention as described and claimed in the above-identified application, prior to the earliest priority date, e.g., July 26, 1993, of U.S. Patent No. 6,605,279.

Other than a general statement of co-inventorship in the Gray Declaration,
the Gray Declaration does not account for the contribution of the co-inventors, given that conception appears to have solely attributed to Gray himself.

Because of this ambiguity, it is incumbent on applicants to provide a satisfactory showing which would lead to a reasonable conclusion that all members of the co-inventorship are the inventors of the claimed invention.
To resolve the ambiguity, applicants may file a declaration by the co-inventors.

Because of this ambiguity, it is incumbent on applicants to provide a satisfactory showing, which would lead to a reasonable conclusion that all of the listed co-inventors (Gary Gray, Man Sung Co, Maxmiliano Vasquez, Beatriz Carreno, Abbie Celniker, Mary Collins, Samuel Goldman, Andrea Knight, Denise O'Hara, Bonita Rup, Geertruida Veldman, Garvin Warner and Stuart Friedrich) are the sole inventors of the claimed invention.

10. Claims 145, 147 and 154 stand rejected under 35 U.S.C § 102(e) as being anticipated by Freeman et al. (U.S. Patent No. 6,605,279) (see entire document) essentially for the reasons of record.

Applicant's arguments in conjunction with the Gray 1.132 Declaration, filed 12/04/2008, have been fully considered but have not been found convincing essentially for the reasons of record and that addressed above in Section 8.

The following is reiterated for applicant's convenience.

Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other suppressive agents, including cyclosporin A or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34).

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure

Although the reference is silent about the term "effective amounts", it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in

the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference.

On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference.

Again, applicant is reminded that the instant claims are read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

Applicant's arguments have not been found persuasive.

11. Given applicant's arguments in conjunction with the Gray Declaration, the following New Grounds of Rejection have been set forth.

Claims 145, 147 and 154 stand rejected under 35 U.S.C § 102(b) as being anticipated by Freeman et al. (WO 95/03408) (1449).

Freeman et al. teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD
(see entire document, particularly Therapeutic Uses by Downregulation of Immune Responses on pages 36-38 and Other Therapeutic Reagents on pages 35-36).

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Although the reference is silent about the term "effective amounts", it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable". In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

On this record, it is reasonable to conclude that the same patient is being administered the same active agent by the same mode of administration in the same amount in both the instant claims and the prior art reference.

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Again, applicant is reminded that the instant claims are read on the elected invention, including the elected species of the combination of anti-B7-1 antibodies, anti-B7-2 antibodies and cyclosporin or rapamycin in the claimed methods are under consideration in the instant application.

12. Given applicant's arguments in conjunction with the Gray Declaration, the following New Grounds of Rejection have been set forth.

Applicant's arguments in conjunction with the Gray 1.132 Declaration, filed 12/04/2008, have been fully considered but have not been found convincing essentially for the reasons of record and that addressed above in Section 8.

Claims 145, 147 and 149-154 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freeman et al. (U.S. Patent No. 6,605,279) OR Freeman et al. (WO 95/03408) (1449).
in view of the well known use of immunosuppressives such as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made, as taught by de Boer et al. (U.S. Patent No. 5,757,034) (1449) essentially for the reasons of record and that addressed above in Section 8.

Applicant's arguments have not been found persuasive.

The following is reiterated for applicant's convenience.

Freeman et al. (U.S. Patent No. 6,605,279) teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Other Therapeutic Reagents on columns 32-34).

Freeman et al. (WO 95/03408) teach methods of downregulating or suppressing T cell mediated immune responses, including the use of B7-1-specific and B7-2-specific antibodies in conjunction with other immunomodulating reagents such as cyclosporine or FK506, including it usefulness in situations of tissue and organ transplantation as well as GVHD (see entire document, particularly Therapeutic Uses by Downregulation of Immune Responses on pages 36-38 and Other Therapeutic Reagents on pages 35-36).
(see entire document, particularly pages 35-38).

While both Freeman et al. references teach the administration of therapeutically effective amounts of the therapeutic compositions, wherein amounts of effective dosages are administered for periods of time necessary to achieve the desired results (e.g. see Administration of Therapeutic Forms of B Lymphocytes Antigens on columns 37-39 or pages 35-38), Freeman et al. differs from the claimed methods by not disclosing the well known use of immunosuppressives such as rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made .

De Boer et al. teach the use of B7-specific antibodies in combination with immunosuppressive agents such as cyclosporin, FK506 and rapamycin (e.g., see column 14, paragraphs 2-3) in therapeutic amounts and modes of administration encompassed by the claimed invention (e.g., see column 16, paragraph 5) (see entire document).

One of ordinary skill in the art at the time the invention was made would have been motivated to modify the teachings of Freeman et al. to incorporate the well known use of immunosuppressives such as as cyclosporin, FK506 and rapamycin and effective therapeutic antibody dosages in transplantation therapeutic regimens at the time the invention was made to achieve the desired therapeutic result of inhibiting graft rejection and promoting long term graft survival with effective amounts of standard immunosuppressives and effective amounts of therapeutic antibodies. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Also, as to the use of a combination of immunosuppressive therapy in transplantations therapeutic regimens, methods of administration are a result effective variable.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 145, 147, 149-154 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claims 1-61 of U.S. Patent No. 6,827,934, and

over claims 1-18 of U.S. Patent No. 6,984,383 (1449; #AA).

The patented claims drawn to methods of therapeutic regimens of transplantation with B7-specific antibodies either anticipate or render obvious the instant claims.

Also, as to the use of a combination of immunosuppressive therapy in transplantations therapeutic regimens or timing of administration of immunosuppressive agents during transplantation regimens,

methods of administration are a result effective variable and immunosuppressive therapy including rapamycin were routine at the time the invention was made by the ordinary artisan.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

15. Claims 145, 147, 149-154 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of USSN 11/294,680.

The copending claims drawn to the same nor nearly the same methods of therapeutic regimens of transplantation with B7-specific antibodies that either anticipate or render obvious one another.

Also, as to the use of a combination of immunosuppressive therapy in transplantations therapeutic regimens or timing of administration of immunosuppressive agents during transplantation regimens,
methods of administration are a result effective variable and immunosuppressive therapy including rapamycin were routine at the time the invention was made by the ordinary artisan.

It is well settled that "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." In re Boesch, 617 F.2d 272, 276, 205 USPQ 215, 219 (CCPA 1980). See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989) (determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious).

16. Claims 145, 147, 149-154 are directed to an invention not patentably distinct from
from claims 1-61 of commonly assigned U.S. Patent No. 6,827,934;
from claims 1-18 of commonly assigned U.S. Patent No. 6,984,383 (1449; #AA) and
from claims 1-9 of commonly assigned USSN 11/294,680
for the reasons above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP Chapter 2300). Commonly assigned U.S. Patent No., discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications pending on or after December 10, 2004.

17. No claim allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phillip Gambel/
Primary Examiner
Art Unit 1644
Technology Center 1600
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